Citation:

Pérez-Jiménez F, López-Miranda J, Pinillos MD, Gómez P, Paz-Rojas E, Montilla P, Marín C, Velasco MJ, Blanco-Molina A, Jiménez Perepérez JA, Ordovás JM. A Mediterranean and a high-carbohydrate diet improve glucose metabolism in healthy young persons. *Diabetologia.* 2001 Nov; 44(11): 2,038-2,043.

PubMed ID: 11719836

Study Design:

Randomized Controlled Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To investigate the effects of a monounsaturated fatty acid-rich (MUFA) diet (similar to the Mediterranean diet) and a low-fat, high-carbohydrate diet on glucose metabolism in young subjects.

Inclusion Criteria:

- Normolipidemic (total cholesterol less than 5.2mmol per L)
- Younger than 30 years of age
- No evidence of chronic illness or unusually high values of physical activity.

Exclusion Criteria:

Subjects with evidence of dyslipidemia, chronic illness or unusually high levels of physical activity.

Description of Study Protocol:

Recruitment

Subjects were volunteers from the University of Cordoba where the study was being conducted.

Design

- RCT to examine the effect of either high MUFA diet or low-fat, high-carbohydrate (CHO) diet on altered glucose metabolism
- Initial 28-day period of subjects on a high SFA diet [15% protein; 47% CHO; 38% fat (20%

SFA, 12% MUFA, 6% PUFA)]
- Participants randomized in a cross-over design and exposed to two new dietary periods:
  - High-MUFA diet (28 days)
    - 15% E as protein; 47% CHO; 38% fat (less than 10% SFA, 22% MUFA, 6% PUFA)
    - Olive oil was 75% of MUFA intake
  - Low-fat, high CHO diet (CHO diet) (28 days): 15% protein; 57% CHO; 28% fat (less than 10% SFA, 12% MUFA, 6% PUFA).

Dietary Intake/Dietary Assessment Methodology

- Composition of the experimental diets was calculated using the USDA food tables or the Spanish food composition tables for local foods
- Lunch and dinner were consumed in the hospital dining room and breakfast in the Medical School cafeteria
- Dietary compliance was evaluated by examining the food diaries and by analyzing the fatty acid content of LDL cholesterol esters.

Blinding Used

Assumed.

Statistical Analysis

- Statistical analyses carried out using the SPSS statistical package
- ANOVA for repeated measures was used to analyze the differences in plasma lipid, glucose, SSPG values and basal glucose and insulin-stimulated glucose uptake between dietary phases
- When statistically significant effects were observed, Tukey's post-hoc test was used to identify differences between groups
- Correlation analysis was done with Pearson's correlation coefficient.
- A P-value of less than 0.05 considered statistically significant.

Data Collection Summary:

Timing of Measurements

- Blood samples were collected after a 12-hour overnight fast at the end of each dietary period
- Each analysis was done three times.

Dependent Variables

- Serum insulin, glucose, lipid and lipoprotein analysis were measured by standard assays
- Glucose suppression test: Test ability of infused insulin to promote disposal of infused glucose; somastatin is also infused to inhibit endogenous insulin secretion
- Glucose uptake by monocytes: Measurement of labeled 2-deoxyglucose (tritiated 2-DG) uptake by isolated monocytes.

Independent Variables

High MUFA or high CHO diets.

Control Variables

Crossover design.

Description of Actual Data Sample:

- *Initial N:* 59 subjects; 30 males, 29 females
- *Mean age:* 23.1±1.8 years
- *Ethnicity:* Spanish
- *Other relevant demographics:* All subjects were students at the University of Cordoba
- *Anthropometrics:* Anthropometrics were the same in the randomized volunteers in the crossover study
- *Location:* Spain.

Summary of Results:

Variables	High SFA Baseline	CHO Diet	High MUFA Diet
	Mean plasma values ±SD	Mean plasma values ±SD	Mean plasma values ±SD
Triglycerides (mmol per L)	0.77±0.3	0.78±0.2	0.79 ±0.3
Total cholesterol (mmol per L)	4.27±0.6[ab]	3.67±0.7	3.74±0.7
HDL-cholesterol (mmol per L)	1.12±0.3[ab]	0.99±0.2	1.03 ±0.2
LDL-cholesterol (mmol per L)	2.80±0.5[ab]	2.32±0.5	2.34±0.6
Fasting glucose (mmol per L)	4.89±0.3[ab]	4.87±0.4	4.79±0.4
Fasting insulin (UI per L)	32.3±9.3[ab]	13.8±5.2	14.7±8.5
Fasting free FA (mmol per L)	0.52±0.3[ab]	0.37±0.2	0.37±0.2
Mean glucose in SSPG	8.06±4.09[ab]	6.61±3.09	6.25±3.08

[a]P<0.001 CHO diet.

[b]P<0.001 High MUFA diet.

In comparison to the SFA diet, both the CHO diet and high MUFA diet:

- Induced a decrease in LDL-C (P<0.001) and HDL-C (P<0.001)
- Decreased steady-state plasma glucose (P=0.023)
- Increased basal and insulin-stimulated 2-DG uptake in peripheral monocytes
- Fasting free FA (FFA) levels in the blood were correlated positively with steady state plasma glucose (R=0.45; P<0.0001).

Author Conclusion:

- Isocaloric substitution of carbohydrates and MUFA for SFA improved insulin sensitivity *in vivo* and *in vitro*, with an increase in glucose disposal
- Both diets were adequate alternatives for improving glucose metabolism in healthy young men and women.

Reviewer Comments:

None.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes

2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	N/A
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes

5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes

8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	Yes
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes